Institutional Development Award (IDeA) Program
CENTERS OF BIOMEDICAL RESEARCH EXCELLENCE (COBRE)
Directory of Active Awards by State and Programs
July 2006

IDeA-Eligible States:

Alaska	Kansas (5)	Montana (3)	North Dakota (3)	South Dakota (2)
Arkansas (2)	Kentucky (6)	Nebraska (4)	Oklahoma (6)	Vermont (2)
Delaware (4)	Louisiana (8)	Nevada (2)	Puerto Rico (2)	West Virginia (3)
Hawaii (2)	Maine (2)	New Hampshire (2)	Rhode Island (4)	Wyoming (2)
Idaho (2)	Mississippi (2)	New Mexico (2)	South Carolina (4)	

Alaska

Center for Alaska Native Health Research
University of Alaska – P20 RR016430

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Thematic Scientific Focus:
Health disparities experienced by Alaska natives, focusing on obesity, nutrition, and cardiovascular disease, investigated from a genetic, dietary, and cultural-behavioral perspective

Representative Research Projects:
- Genetics of obesity
- Cultural understandings of health
- Diet and nutrition knowledge

Research Resources:
- Epidemiology, biostatistics and bioinformatics core
- Genetics core
- Culture and behavioral research core
- Community outreach services

Index Terms:
health disparities, nutrition, obesity, epidemiology, bioinformatics, genetics

back to top

Arkansas

Center for Protein Structure and Function
University of Arkansas at Fayetteville – P20 RR015569

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Thematic Scientific Focus:
Structure and function of biomedically important proteins, including bacterial, viral, and membrane-associated proteins, with emphasis on structure-based drug discovery and design

Representative Research Projects:
- Protein interactions with the extracellular matrix
- Structure-based drug discovery
- Protein targeting
- Principles of protein folding and design
- Membrane Proteins

Research Resources:
- NMR core – 500 MHz and 700 MHz NMR spectrometers with cryoprobes; 300 MHz solid-state NMR spectrometer for membrane proteins
- X-ray crystallography core – two Rigagku diffractometers with Saturn92 CCD detectors; robotic protein crystallization facility
- Mass spectrometry core – IonSpec 9.4 Tesla FTMS Fourier transform mass spectrometer equipped with MALDI and ESI sources; five other mass spectrometers
- Large-scale protein production facility – four Applikon bioreactors and ancillary equipment; Applied Biosystems protein sequenator, and peptide synthesizer; Beckman analytical and preparative ultracentrifuges
- High-throughput synthesis core – Bruker Avance 300 MHz NMR; CEM Explorer automated microwave synthesis workstation; eight Radley 12-vessel parallel synthesizers, and associated supporting instrumentation

Index Terms:
NMR, structural biology, mass spectrometry, x-ray crystallography, drug design, protein targeting

Center for Translational Neuroscience
University of Arkansas for Medical Sciences – P20 RR020146

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Thematic Scientific Focus:
Establishment of a broad-based translational neuroscience research center

Representative Research Projects:
- Comprehensive assessment of motion sickness and neurovestibular disorders
- Chronic low back pain and depression
- Pain: early experience and pre-attentional mechanisms
- Palliative strategies for spinal cord injury
- Cytoplasmic polyadenylation-mediated control of mRNA translation in neurogenesis and neuropathology

Research Resources:
- Electrophysiology core – psychomotor vigilance task instrumentation; transcranial magnetic stimulation system
- Image analysis core – confocal microscope; fluorescent and light microscopic systems
- Molecular biology core
- Transcranial magnetic stimulation core Facility

Index Terms:
neurological disorders, chronic pain, spinal cord injury, neurogenesis, neuropathology

back to top

Delaware

Design of Hierarchical Recognition Motifs
University of Delaware – P20 RR017716

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Thematic Scientific Focus:
Development of molecular recognition elements for structural control in macromolecules, encompassing atomic-level interactions among small molecules, proteins, and multi-protein assemblies

Representative Research Projects:
- Small molecule alpha-helix mimics
- Peptide-based biomaterials with environ-sensitive morphologies
- Strained molecules for synthesis of unnatural amino acids
- Artificial glycoproteins for applications in materials and biology
- Determinants of stability and assembly of integral membrane proteins
- Protein assemblies and metalloproteins

Research Resources:
- Protein production and purification core
- Peptide/protein NMR core – 600 MHz NMR spectrometer with cryoprobe; 300 MHz solid-state NMR spectrometer for membrane proteins
- X-ray crystallography core
- Mass spectrometry core
- Networked computational facility – Linux computer cluster for molecular modeling

Index Terms:
proteins, recognition motifs, molecular topology, unnatural amino acids, protein engineering, materials science, chemical engineering, biomaterials

Osteoarthritis: Prevention and Treatment
University of Delaware – P20 RR016458

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Thematic Scientific Focus:
Mechanisms, prevention, and treatment of osteoarthritis, focusing on cartilage healing and the biomechanics of the human knee

Representative Research Projects:
- Healing of cartilage after experimentally induced osteoarthritis
- The osteoarthritic knee: a biomechanical analysis
- Effect of in-shoe wedges on knee osteoarthritis
- Correction of genu varum deformity by an opening wedge osteotomy

Research Resources:
- Magnetic resonance imaging core
- Computational modeling core
- Clinical diagnostic and treatment facilities – surgical facilities; advanced equipment for testing and measuring material properties of tissues, muscle activation patterns, muscle performance, and limb motion
- Gait laboratories – six-camera systems with multiple force plates and EMG data acquisition capability; functional electrical stimulation equipment; biomechanical modeling; robotic-assisted training systems

Index Terms:
biomechanics, orthopedics, physical therapy, magnetic resonance imaging, electromyography, tissue engineering, gait analysis

Center for Pediatric Research
Alfred I. duPont Hospital for Children – P20 RR020173

Principal Investigator:
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Thematic Scientific Focus:
Establish a translational research center to study pediatric disorders, create corresponding therapies, and develop new and better methods of prevention

Representative Research Projects:
- Developmental mechanisms of undescended testis
- Molecular mechanisms in Pelizaeus Merzbacher disease
- Peripheral nervous system in cerebral palsy
- Extracellular matrix remodeling in cardiovascular diseases
- Mechanisms of cell death in spinal muscular atrophy
- Oxygen and barotrauma effects on human airway epithelium

Research Resources:
- Clinical Research Services – support and oversight for research studies involving human subjects and clinical trials
- Cell Science Core – services and resources for preparative and analytical studies for cell biology, protein biochemistry and molecular biology

Index Terms:
pediatric diseases, neurological disorders, cell death, cardiovascular diseases

COBRE on Membrane Protein Production and Characterization
University of Delaware – P20 RR015588

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Thematic Scientific Focus:
To express, solubilize, purify and crystallize membrane proteins, to determine their structures, and to characterize their functions at the molecular level and in larger biological systems

Representative Research Projects:
- Determinants of GPCR expression in *E. coli* and yeast and of solubilization and stability
- Structure and interfacial function of platelet activating factor acetylhydrolase
- The role of JAM-A in cancer metastasis and spermatogenesis
- Characterization of plasmodesmal channel protein

Research Resources:
- Protein production and purification core
- Biophysical characterization core
- Protein X-ray crystallography facilities
- Bioimaging core – multiphoton confocal microscopes; electron and scanning probe microscopy; laser capture microdissection system

Index Terms:
genomics, proteomics, mass spectrometry, bioinformatics, molecular biology, protein chemistry, cancer, cardiovascular disease, x-ray diffraction, crystallography, chemical warfare agents, asthma, allergies, arthritis, inflammation, cystic fibrosis, Alzheimer's disease, prion diseases

back to top

Hawaii

COBRE Center for Cardiovascular Research
University of Hawaii – *P20 RR016453

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Thematic Scientific Focus:
Molecular and cellular mechanisms underlying human cardiovascular diseases, with emphasis on structural, biochemical, and genetic studies in cell culture and animal model systems

Representative Research Projects:
- Connexin43 regulation in proliferative vascular disease cancer
- Modulating effect of hyperglycemia on cerebral ischemia
- Solid state NMR studies of mineralized elastin
- Pathogenetics of recessive pseudoxanthoma elasticum (PXE)
- Elastin and elastin receptor in vascular diseases
- Proteins responsible for integrin-mediated cell survival

Research Resources:
- Genomics and bioinformatics core – DNA sequencing, SNP genotyping, and whole-genome expression profiling; computer cluster for high-throughput data processing
- Histology and confocal microscopy core – specialized immunohistochemistry services

Index Terms:
cardiovascular disease, intercellular communication, gap junctions, receptor-mediated signaling cascades, cell biology, genetics, elasticity of connective tissue and smooth muscle

Pacific Center for Emerging Infectious Diseases Research
University of Hawaii at Manoa – P20 RR018727

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Thematic Scientific Focus:
The emergence and spread of newly recognized infectious diseases with special attention paid to those diseases that disproportionately affect under-served ethnic minorities and disadvantaged or marginalized communities in Hawaii and the Asia-Pacific region

Representative Research Projects:
- Molecular epidemiology and natural history of human papillomavirus in men
- Immunopathogenesis of dengue virus infection
- Group A Streptococci in relation to acute rheumatic fever in Hawaii

Research Resources:
- Technical support core – FACS flow cytometry; cell sorting; real-time PCR analysis; DNA sequencing; Affymetrix gene chip DNA microarray analysis; metabolomics; bioinformatics
- BSL-3 containment facility

Index Terms:
infectious diseases, emerging diseases, health disparities, epidemiology, evolution, group A streptococci, dengue virus, human papillomavirus

back to top

Idaho

Center for Research on Processes in Evolution
University of Idaho – P20 RR016448

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Thematic Scientific Focus:
Role of mutagenic processes on the tempo and trajectory of adaptive evolution, emphasizing the evolutionary history of functional domains in microbial proteins, structural genes, and genomes

Representative Research Projects:
- Predictability of viral evolution
- Evolution of antibiotic resistance plasmids
- Evolution of protein flexibility
- Computational and mathematical analysis of biomedical data

Research Resources:
- Molecular biology core – DNA cloning and sequencing; protein expression and purification; computer workstations and software for molecular modeling
- Bioinformatics core –Bioinformatics Core - Three Beowulf Supercomputers: 54 node with 54 processors; 134 node with 268 processors; and 50 node with 100 processors
- Structural biology core – 600 MHz NMR spectrometer; cell-culture systems for preparative-scale protein labeling with stable isotopes

Index Terms:
evolutionary biology, molecular biology, structural biology, microbial ecology, computational biology, statistics, genomics, proteomics

Molecular and Cellular Basis of Host-Pathogen Interaction
University of Idaho – P20 RR015587

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Thematic Scientific Focus:
Molecular and cellular basis of host-pathogen interactions, emphasizing microbial pathogenesis

Representative Research Projects:
- Potassium sensing by the obligate intracellular parasite *Toxoplasma gondii*
- The impact of lipid metabolism on *staphylococcal mastitis*
- Human cytomegalovirus interactions with cellular p53
- Investigation of the *Y. pestis* immune evasion response to human neutrophils
- Maintenance of hyphal polarity by DopA protein and its role in *Aspergillus* pathogenesis
- Role of Hsp90 in polarized cell morphogenesis in *S. cerevisiae* and *C. albicans*
- Transcriptional attenuation of the type I interferon response by rhinovirus

Research Resources:
Molecular biology core – DNA cloning and sequencing; protein expression and purification; computer workstations and software for molecular modeling
- Bioinformatics core – 64-node Beowulf cluster supercomputer
- Structural biology core – 600 MHz NMR spectrometer; cell-culture systems for preparative-scale protein labeling with stable isotopes
- BSL-3 facility – certified and registered by the Centers for Disease Control and Prevention
- Cell Separation core – FACSCalibur flow cytometer, Becton Dickinson FACSAria flow cytometer/cell sorter, PALM Microbeam laser microdissection system with epifluourescent capability

Index Terms:
molecular biology, cell biology, pathogens, *E. coli*, antiviral, immunology, *Staphylococcus*, gangrene, colitis, microbiology, virology, sexually transmitted diseases, HIV, trauma, antibiotic resistance, *Clostridium*, *Yersinia pestis*, Toxoplasma, mastitis, immunocompromised, invasive Aspergillosis, neutrophil, rhinovirus, human cytomegalovirus

back to top

Kansas

Center for Cancer Experimental Therapeutics
University of Kansas, Lawrence - P20 RR015563

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Thematic Scientific Focus:
Cancer-related research at the interface between chemistry and biology, focusing on identifying novel bioactive compounds for use as basic biomedical research tools and new therapeutic agents

Representative Research Projects:
- A novel stem cell source for cancer therapy
- Nuclear functions for the tumor suppressor protein APC
- dsRNA as a novel cancer therapeutic: mechanism for systematic RNAi
- Novel peptide inhibitors of breast tumor growth
- Roles of NRP-1 in breast cancer development
- Functions of Rho: regulator of development and metastasis
- Protease inhibitors for cancer therapy
- Weight control, cell signaling and cancer prevention

Research Resources:
- High throughput screening and target identification core – robotic bioassay system for screening chemical libraries; custom chemical and biomolecular structure databases
- Medicinal chemistry core – combinatorial organic chemistry; custom synthesis and purification of small-molecule libraries of enzyme inhibitors

Index Terms:
medicinal chemistry, combinatorial chemistry, bioassays, molecular library screening, drug design, cancer, oncology, cell biology, molecular biology, retrovirus

Center for Epithelial Function in Health and Disease
Kansas State University College of Veterinary Medicine – P20 RR017686

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Thematic Scientific Focus:
Epithelial function in health and disease, emphasizing epithelial cell physiology and pathophysiology to create a strong foundation for translational research

Representative Research Projects:
- Transepithelial ion transport and its regulation
- Renal, reproductive, mammary and intestinal epithelia
- Molecular basis of migration pathology in intestinal epithelia caused by non-steroidal anti-inflammatory drugs
- Molecular basis of protein and vesicle traffic in epithelia
- Interactions between pathogens and arthropod midgut epithelial cells
- Canine urogenital beta-defensins, a novel family of epithelium-derived antimicrobial peptides

Research Resources:
- Confocal microfluorometry – Zeiss LSM510 Meta, microfluorometry of fast Ca2+ signals in cultured and native epithelial tissues; subcellular visualization and co-localization of fluorescently labeled molecules; Leica CM3050 S cryostat; Zeiss/PALM laser catapulting dissection microscope
- Molecular biology core – DNA sequencing; quantitative RT-PCR; DNA microarrays and related equipment for gene expression profiling; protein analysis support (mass spec)
- Epithelial electrophysiology core – tools for noninvasive current and nonradioactive ion flux measurements, including self-referencing ion-selective electrodes, vibrating current-density probes

Index Terms:
epithelium, electrophysiology, molecular biology, gene expression, ion transport, pharmacology, cellular regulation

COBRE in Protein Structure and Function
University of Kansas School of Pharmacy, Lawrence – P20 RR017708

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Thematic Scientific Focus:
Protein structure-function relationships at the atomic and molecular level

Representative Research Projects:
Allosteric determinants in the LacI/GalR family
The structural biology of pyoverdin biosynthesis
Structure and function of bacterial prolyl-4-hydroxylase
Structure-function of mammalian cytochromes P450
Structure and mechanism of CS1 pilus assembly
Redox effects on the structure and dynamics of PRL-1
Protein-protein recognition involved in hematopoiesis

Research Resources:
- Protein structure laboratory – protein crystallization and X-ray data collection and analysis; structure solution and refinement
- Protein chemistry and analysis laboratory – preparative scale production and purification of proteins; protein binding assays including surface plasmon resonance; protein mass spectrometry; 2-D gel electrophoresis

Index Terms:
protein structure, proteomics, mass spectroscopy, allostery, transcriptional activation, protein interactions, chaperones, glycoproteins, membrane proteins, signal transduction, medicinal chemistry, rational drug design

Novel Approaches for Control of Microbial Pathogens
University of Kansas – P20 RR016443

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Thematic Scientific Focus:
Novel molecular mechanisms for inhibiting replication of pathogenic microbes, emphasizing immunopathological responses to infectious agents and host antigens

Representative Research Projects:
- Structure-function relationship of antibiotic targets MurA and EPSP synthase
- Bacterial cell division proteins as targets for antimicrobials
- Antimicrobials targeted to M protein of Streptococci
- Purification and crystal structure of a novel baculovirus RNA polymerase subunit
- Pseudomonas Type 3 effector protein AvrPto in pathogenesis: host defense
- Immunogenicity of HIV DNA vaccines and cytokines in mice
- Roles of p30 in HTLV-1 latency
- HCV NS5B polymerase mutations: biology/pharmacology
- Development of peptidyl nucleosides as novel antifungals
- Lyme borreliosis and babesial coinfection
- CAEV/SHIV chimera for studies on bystander death of CD4+ T cells in goats
- Faculty Recruitment Enhancement Projects:
  - HHV-8 envelope glycoprotein gB as a target for novel therapeutic agents
  - Structure-function analysis of *Borrelia* vsp and vlp surface lipoproteins
  - Synthesis of novel C-5' modified nucleoside analogs
  - Gene therapy of TB granulomas in mice
  - Breaking HTVL-1 latency: p30-RNA interaction as a novel therapeutic target
  - Characterization of the novel *Enterococcus faecalis* protein EBSG in lipoteichoic acid structure and function
  - Siderophore production and import in *Pseudomonas aeruginosa*
  - Hepatitis C virus in NS5B polymerase
  - Genetics of capsular polysaccharide production in *Enterococcus faecalis*
  - Effect of hemifluorinated surfactants on membrane insertion/folding of diphtheria toxin T domain
  - Regulation of CCR7-mediated adhesion of T cells through LFA-1
  - The Gads adaptor protein in T cell-mediated prevention of viral pathogenesis
  - Early gene expression curing T cell activation
  - Cytotoxic necrotizing factor 1 in *E. Coli* Meningitis
  - High resolution structure of herpesvirus

Research Resources:

- X-ray crystallography core – protein crystallization and structure determination; high-throughput screening of small-molecule libraries; molecular modeling; structure-based drug design
- Fermentation and screening core – preparative scale production and purification of native and engineered proteins
- Flow Cytometery Core – identification of cells of the immune system that are involved with development of specific immune responses
- Luminex Core – provides a mechanism for measuring minute quantities of cytokines and chemokines produced by cultured immune cells
- Signal Transduction Core – provides a mechanism for identifying molecular pathways involved in production of viral proteins in infected cultures and in generating host responses

Index Terms:

pathogens, microbial infection, molecular structure, protein X-ray crystallography, mechanism-based enzyme inhibitors, drug development, cell mediated immune responses, development of the immune system

Nuclear Receptors in Liver Health and Disease
University of Kansas, Lawrence - P20 RR021940

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Thematic Scientific Focus:
Nuclear Receptors and their role in liver health and disease

Representative Research Projects:
- The role of organic anion transporting polypeptides (OATPs) in nuclear receptor activation
- Mechanisms by which farnesoid-x-receptor (FXR) alters hepatic lipid metabolism and decreases fatty liver development
- Role of SHP (small heterodimer partner) in fatty liver
- Physiological function of nuclear receptors in cholestatic liver diseases
- Identification and functional characterization of SNPs (single nucleotide polymorphisms) in RXRα (retinoid-x-receptor α) gene

Research Resources:
- Molecular biology core – DNA Sequencing; real time PCR including reagents; high throughput PCR for rapid genotyping; a vector, plasmid, and bacteria bank
- Null-mouse development and husbandry core
- Phenotyping/pathology core –serum chemistries and immunohistochemistry
- Analytical core – HPLC, LC-MS/MS, FPLC, and multi-mode spectrophotometry.

Index Terms:
nuclear receptors, ligands, transporters, drug interactions, hepatic diseases, lipid metabolism

back to top

Kentucky

Center for the Biologic Basis of Oral/Systemic Diseases
University of Kentucky, College of Dentistry – P20 RR021045

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Thematic Scientific Focus:
The biological principles that underlie the apparent linkage among chronic oral infections, inflammation, and systemic disease sequelae, with an emphasis on translational studies of host-parasite interactions and on clinical implications for systemic disease

Representative Research Projects:
- Oral infections and HIV recrudescence
- Cox-2 and 12/15-LO in atherosclerosis
- Impact on gestational diabetes
- Dietary regulation of local and systemic inflammatory responses
- Viral/bacterial infections in chronic disease
- Smoking: effect of genotype on periodontitis

Research Resources:
- Biostatistics and bioinformatics core – statistical consultation on study design and data analysis
- Transgenic mouse facility
- Microarray core – complete Affymetrix gene chip system

Index Terms:
oral infections, inflammation, translational research, HIV, atherosclerosis, gestational diabetes, periodontal disease

COBRE in Molecular Targets
University of Louisville – P20 RR018733

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Thematic Scientific Focus:
Identification of novel molecular targets for cancer therapy using the techniques of modern structural biology

Representative Research Projects:
- Glycolysis and neoplastic growth
- Development and testing of small molecular antagonists of monocyte/macrophage migration inhibitory factor (MIF) recently found to play an important role in carcinogenesis
- Elucidation of the signaling mechanisms involved in activation-dependent lipid signaling enzyme, sphingosine kinase, and its product, sphingosine-1-phosphate, in control of cell proliferation, survival and migration
- Development of a sequence-specific double-stranded DNA cleaving agent
- Structural studies of TRAF6-mediated IL-1 and Toll-like receptor signaling pathways

Research Resources:
- Microsequence array facility – Affymetrix gene chip instrumentation
- Molecular modeling facility – state-of-the-art modeling projections from structural data obtained through X-ray crystallographic or NMR analysis
- Computational resources - Silicon Graphics array; time on the institution's IBM SP2 supercomputer
- NMR and protein purification facility – 650 MHZ and 800 MHz NMR instruments; comprehensive protein expression laboratory that includes an analytical ultracentrifuge
- Proteomics facility – automated equipment for high-throughput proteomic analysis; robotic workstations for gel throughput, image analysis, spot excision, in-gel peptide digestion and MALDI-TOF sample preparation; mass spectrometry and high resolution 2-D gel analysis

Index Terms:
neoplastic transformation, cancer, molecular targets, signaling pathways, cytokines, growth factors, kinases

COBRE in Women's Health
University of Kentucky – P20 RR015592

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Thematic Scientific Focus:
Roles of female reproductive hormones in manifestations of health and disease in women and in animal model systems

Representative Research Projects:
- Estradiol and testosterone regulation of cardiac injury
- Estradiol and LH-mediated regulation of ovarian function
- Estradiol interactions with the proteosome in HIV regulation
- Interactions of estradiol and antidepressants in hippocampal neurogenesis
- Actions of estradiol and progesterone on behavior: clinical neuropharmacology

Research Resources:
- Magnetic resonance imaging core
- Transgenic mouse core
- DNA microarray core
- Bioinformatics and biostatistics core

Index Terms:
women's health, estrogen, reproduction, cell biology, molecular biology, behavior, steroids, HIV, neurodegenerative diseases, cognition, aging, cancer, ovary, brain

Central Nervous System Injury and Repair
University of Louisville – P20 RR015576

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Thematic Scientific Focus:
Molecular and cellular mechanisms of spinal cord injury and repair, with emphasis on developing and characterizing clinically relevant animal models

Representative Research Projects:
- Methylprednisolone and spinal cord injury: a new approach to an old therapy
- Reconstructing locomotor circuitry after spinal cord injury
- Human olfactory epithelium as a source of stem cells for CNS repair
- Cellular mechanisms of neuronal vulnerability to intermittent hypoxia
- Signaling pathways in neuronal apoptosis

Research Resources:
- Cell culture and molecular biology core – neuronal stem cell culture; FACS analysis; production of viral vectors for gene transfer experiments
- Animal surgery core – gene transfer manipulations; stem cell transplantation; nerve grafting; neuroanatomy analysis
- Animal behavior and electrophysiology core – gait analysis; electropotential recordings *in vivo* and in tissue slices and single cells
- Microscopy core – immunohistochemistry; confocal and light microscopes; transmission and scanning electron microscopes

Index Terms:
neurobiology, cell culture, molecular biology, surgery, behavior, electrophysiology, microscopy, apoptosis, immunology, signaling, central nervous system, spinal cord injury, stem cells

COBRE in the Molecular Basis of Human Disease
University of Kentucky College of Medicine – P20 RR020171

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http://www.mc.uky.edu/biochemistry/cobre/default.asp

Thematic Scientific Focus:
The molecular basis of human disease, with an emphasis on examining the role of altered gene expression and protein processing on promoting the diseased state

Representative Research Projects:
- Mechanism of transcriptional control by two diabetes gene products
- Talin-1 metastasis suppressor in lung cancer
- PDGF signal transduction: Role for Abi family kinases in cell migration
- Dissecting the cell surface proteome of prostate cancer
- Therapeutics in a mouse model of inclusion body myositis

Research Resources:
- Tissue culture and protein production core – tissue culture hoods and incubators for mammalian cell culture; fermenters, bioreactors, cell cracking equipment, and chromatography instrumentation for production of recombinant proteins
- Imaging core – three epifluorescence microscopes (Nikon Eclipse 600, Zeiss Axiovert 100 and 200M) with digital image capture capability (Spot CE and Orca ER digital cameras with Metaview and Open Lab software)
- Proteomics core – quantitative and qualitative protein profiling and identification analysis, as well as post-translational modification and sequence analysis through a combination of 2D gel, mass spectrometry and Edman sequencing analysis services; equipped with Bio-Rad IPG and SDS-PAGE apparatus for 2D gel analysis, a Typhoon phosphorimager/scanner system for detection and quantitation of fluorescent protein dyes, a Ciphergen SELDI-TOF protein profiling system, an ABI QSTAR II Q-TOF mass spectrometer with both MALDI and LC/ESI source capabilities, Waters HPLC systems and multiple PCs for data acquisition and analysis including a site license for PDQuest software and a five station site license for Ciphergen software

Index Terms:
transcriptional regulation, cancer genes, signal transduction, diabetes, prostate cancer

Molecular Determinants of Developmental Defects
University of Louisville School of Dentistry – P20 RR017702

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http://www.louisville.edu/hsc/birthdefectscenter/cobre/index.htm

Thematic Scientific Focus:
Molecular and cellular mechanisms controlling normal embryonic development and etiology of birth defects

Representative Research Projects:
- TGF-beta and Wnt signaling: cross-talk during craniofacial development
- An antioxidant transgene protects offspring from maternal diabetes
- The c-ski transcriptional regulator of neural tube ontogenesis: effects on the cranial neural crest
- Developmental processes of pituitary differentiation and maturation
- The role of TFII-I transcription factor in neural tube closure defects
- *GATA4* and *NKX2.5* mutations in patients with congenital heart disease
- Measurement issues associated with cerebral tissue oxygenation in preterm infants
- Biomarkers of tobacco exposure *in utero*: correlations with altered gene expression
- Inositol signaling and brain disorders
- The use of Cre/loxP system to study the role of germ cell nuclear factor

Research Resources:
- DNA and microarray cores – DNA sequencing; mutation and SNP detection; custom microarray fabrication and analysis; gene expression profiling
- Laser capture microdissection
- Protein mass spectrometry core – protein purification and sequencing; MALDI-TOF and ESI mass spectrometers
- Animal care and transgenic mouse cores
- Biostatistics core

Index Terms:
birth defects, developmental biology, embryogenesis, gene expression, signal transduction, craniofacial disorders, diabetes, neural tube defects, cardiovascular defects

back to top

Louisiana

Center for Experimental Infectious Disease Research
Louisiana State University – P20 RR020159

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http://www.labiomed.info/

Thematic Scientific Focus:
The immunological and pathogenetic basis of infectious diseases

Representative Research Projects:
- TNF & MCP-1 in retrovirus induced brain disease
- Monocyte infection in SIV neuropathogenesis
- Early RSV exposure leads to adult airway disease
- Host response in HIV-1 & microsporidia coinfection
- Pathogenesis of new SIVsm lineages in rhesus macaques

Research Resources:
- Molecular Biology Core – providing DNA sequencing; library construction; microarray analysis; FACS analysis; and confocal microscopy
- Non-human primate and laboratory core

Index Terms:
infectious diseases, non-human primate models, retrovirus, SIV, RSV, pathogenesis, host response

Center for Molecular and Tumor Virology
Louisiana State University Health Sciences Center – P20 RR018724

Principal Investigator:
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http://www.sh.lsuhsc.edu/cobre

Thematic Scientific Focus:
The molecular mechanisms by which viral gene products alter the cell and orchestrate events leading to disease

Representative Research Projects:
- Role of innate immunity in yellow fever virus pathogenesis
- Polyamine metabolism in Epstein-Barr virus lymphomagenesis
- Role of herpesvirus glycoproteins in severe inflammatory diseases
- Replication of murine norovirus 1 (MNV-1)

Research Resources:
- Cell culture and molecular analysis core – central repository for stocks and cell lines; phosphoimager and FACS flow cytometer/sorter

Index Terms:
virology, infectious agents, molecular pathogenesis, viral oncology

Mentoring a Cancer Genetics Program
Tulane University Health Sciences Center – P20 RR020152

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http://www.som.tulane.edu/cancer/default.html

Thematic Scientific Focus:
To develop a center in cancer genetics and gene regulation with an emphasis on understanding how genetic instability contributes to the initiation and progression of cancer

Representative Research Projects:
- Phosphorylation in solid muscle tumor alveolar rhabdomyosarcoma
- Innovative therapies for T(4;11) leukemia
- ATR kinase and UV-induced cell cycle checkpoints
- Genetic instability, environmental activation of mobile elements
- Environmental cues, mesenchymal stem cells, tumor angiogenesis

Research Resources:
- Cell assay core – employs a series of devices for gene function, expression and mutagenesis assays

Index Terms:
cancer genetics, gene instability, gene regulation, tumors, leukemia, cell cycle, angiogenesis

Mentoring in Cardiovascular Biology
Louisiana State University Health Sciences Center – P20 RR018766

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http://www.medschool.lsuhsc.edu/pharmacology/

Thematic Scientific Focus:
The molecular and physiological basis of cardiovascular function, with particular emphasis on vascular biology and cell signaling as related to vascular disease

Representative Research Projects:
- Role of PARP-1 and oxidative stress in the pathogenesis of atherosclerosis
- Gene transfer, oxidative stress and diabetic vascular disease
- Integration of growth factor and integrin signaling in vascular smooth muscle cells
- ER to Golgi trafficking of signaling proteins in cardiac myocytes and vascular smooth muscle cells

Research Resources:
- Cell and molecular core – cell culture and molecular biology services, such as real time PCR analysis; proteomics work station that provides 2-D gel electrophoresis analysis utilizing laser imaging through the Amersham Typhoon system; spot picker; mass spectroscopy analysis
- Histology core – tissue processing, staining and pathology analysis
- Cardiac and vascular function core – telemetry and *in vivo* ultrasound imaging

Index Terms:
cardiovascular disease, atherosclerosis, MAP kinase signaling, ischemic heart damage, oxidative stress, cell trafficking, G protein-coupled receptors

Mentoring Neuroscience in Louisiana
Louisiana State University Health Sciences Center – P20 RR016816

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http://www.medschool.lsuhsc.edu/neuroscience/

Thematic Scientific Focus:
Cellular and molecular basis of neurological plasticity and survival in the contexts of stroke, neuronal trauma, and neurodegenerative diseases

Representative Research Projects:
- System A transporters in glutamatergic neurotransmission
- Mechanisms of acetylcholine plasticity in hypothalamus
- Secreted phospholipases A2 participate in neuron survival
- Cyclooxygenases in neuronal synaptic plasticity

Research Resources:
- Molecular neurobiology core – data imaging and quantitation systems; custom DNA microarray production and analysis; transgenic mouse maintenance and genotyping
- Neurochemistry core – characterization of lipid messengers structure and metabolism by TLC, HPLC, GLC, LC-MS/MS
- Imaging core – two-photon laser scanning microscope, laser scanning confocal microscope, upright electrophysiology microscope with high-speed CCD camera

Index Terms:
neuroscience, stroke, neurological trauma, neurodegenerative diseases, imaging, molecular biology, cell biology

Mentoring Oral Health Research in Louisiana
Louisiana State University School of Dentistry – P20 RR020160

Principal Investigator:
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http://www.lsusd.lsuhsc.edu/research/center_grants.htm

Thematic Scientific Focus:
Oral infectious diseases, including projects that focus on oral health anomalies, including oral opportunistic infections in the HIV patient, periodontal disease, and dental caries

Representative Research Projects:
- Development of new adhesive fluoride-releasing monomers
- Effect of aging on periodontal disease
- Role of vacuole expansion in the oral pathogen *Candida albicans*
- Mechanisms behind CX3CL1-driven monocyte recruitment during periodontitis

Research Resources:
- Biomedical equipment core – equipment and expertise to carry out periodontal protocols
- Statistical core – support in the areas of study design, sample size estimation/statistical power analyses, statistical methodology and database management

Index Terms:
Oral health, oral infectious diseases, periodontal disease, HIV

Mentoring Translational Researchers in Louisiana
Louisiana State University Health Sciences Center – P20 RR021970

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http://www.medschool.lsuhsc.edu/cancer_center/research.asp

Thematic Scientific Focus:
To understand the immunobiology of disease; specifically, investigations focus on elucidating and subsequently controlling the mechanisms that lead to chronic inflammation and tissue damage during disease

Representative Research Projects:
- Tolerance mechanisms in head and neck cancer and approaches to overcome them
- Overcoming tumor tolerance through *in vivo* generated dendritic cells
- Alterations in T cell signal transduction caused by chronic inflammation in steroid-resistant idiopathic nephrotic syndrome
- Dendritic cells and immune response in corneal tissue
- Manipulation of lymphocyte homeostasis for enhancing anti-tumor immunity

Research Resources:
- Immunology and cell analysis core – flow cytometry, cell sorting and cell separation services
- Microarray and sequencing core – low cost sequencing and GeneChip preparation and analysis services
- Biostatistics core

Index Terms:
inflammation, host defense, immune response, T cells

Tulane Hypertension and Renal Center of Excellence
Tulane University School of Medicine – P20 RR017659

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http://www.som.tulane.edu/centprog/htn/COBRE.htm

Thematic Scientific Focus:
Factors contributing to development of hypertension and subsequent consequences on renal and cardiovascular function

Representative Research Projects:
- Angiotensin receptors in renal microvascular physiology
- Angiotensin in distal nephron ontogeny
- Heme-heme oxygenase-carbon monoxide system in salt-induced hypertension
- Role of genetic polymorphisms in epoxygenase pathway enzymes in hypertension
- Beneficial effects of physical activity on blood pressure in African-American females
- Tubular renin-angiotensin system in hypertension
- Lead and cadmium and kidney disease progression
- Effects of soybean protein on adipocytokines, systemic inflammation, and endothelial dysfunction
- Heme oxygenase in angiotensin II hypertension
- Citrate transport in the proximal tubule
- Endothelial dysfunction, adipocytokines, inflammation and chronic kidney disease

Research Resources:
- Molecular Biology and Analytical Core – RIA; ELISA analyses; gel documentation system for nucleic acids and proteins; gene array analysis and real-time PCR assays; flow cytometry
- Transgenic animal core – rats and mice

Index Terms:
hypertension, blood pressure, renal, angiotensin, polymorphisms, cardiovascular disease, kidney disease

back to top

Maine

COBRE in Vascular Biology
Maine Medical Center Research Institute – P20 RR015555

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http://www.mmcri.org/cmm/vascularCOBRE.html

Thematic Scientific Focus:
Cell and molecular mechanisms regulating development and homeostasis of the vascular system including vascular remodeling, angiogenesis, and disease mechanisms

Representative Research Projects:
- Mechanisms of dyslipidemia in cardiac muscle prior to onset of atherosclerosis
- Control of vascular fibrosis and collagen deposition by novel regulator, CTHRC-1
- The contribution of smooth muscle cells to the pathology of gastrointestinal stromal tumors
- Smad-independent TGF-beta signaling mechanisms in angiogenesis
- Mechanism of non-classical release of the angiogenesis regulator, IL1-alpha

Research Resources:
- Structural biology core – capillary-based automated DNA sequencing; peptide and protein sequencing; protein mass spectrometry with MALDI-TOF and quadrupole tandem mass spectrometers
- Molecular genetics core – transgenic mouse and gene knock-out mouse production; small animal MRI

Index Terms:
structural biology, molecular biology, molecular genetics, angiogenesis, signaling, vascular biology, cancer, inflammation, endothelial cell, vascular smooth muscle cell, atherosclerosis

Center for Regenerative Medicine
Maine Medical Center Research Institute – P20 RR018789

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http://www.mmcri.org/cmm/stemCOBRE.html

Thematic Scientific Focus:
Discovery of novel regulators of stem and progenitor cell proliferation, survival and development (including cell-cell, cytokine receptor, transcription factor and (epi)genetic signals) with clinical relevance to damaged tissue repair

Representative Research Projects:
- Regenerative properties of nephrogenic mesenchyme
- EphB4 regulation of hematopoietic vs endothelial progenitor cell fate
- Genome instability and stem cell function in lymphomyeloid neoplasia
- pMesogenin and cristin/R-spondin regulation of mesodermal differentiation
- Role of WNT signaling in the preimplantation embryo
- Slug factor regulation of hematopoietic progenitor cell survival, and leukemogenesis

Research Resources:
- Progenitor cell isolation and analysis core – supports FACS and preparative MACS isolation of primary cell populations, flow cytometric (and Vicell) analyses; basic murine and human ES cell services
- Bioinformatics and genomics core – supports robotic DNA and RNA isolation, quantitative (RT) PCR, and project specific in silico array analyses
- Histopathology core – provides stained tissue sections via fixation, processing, embedding, sectioning, staining and coverslipping of paraffin or frozen tissue sections; staining ranges from H&E's to specific tissue stains for collagen, amyloid, bone, cartilage, vessels, kidney basement membranes, and hematopoietic cells; the core also offers immunohistochemical staining for general antibody sets

Index Terms:
stem and progenitor cell biology, cytokine signal transduction, nephron mesenchyme, endothelial, EphB4, R-spondin, mesoderm, genomic instability, hematopoiesis, leukemogenesis, Wnt signaling

back to top

Mississippi

Center for Psychiatric Neuroscience
University of Mississippi Medical Center – P20 RR017701

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http://cpn.umc.edu/

Thematic Scientific Focus:
Psychiatric neuroscience geared toward improving the diagnosis and treatment of psychiatric illnesses such as depression, schizophrenia, and substance abuse disorders

Representative Research Projects:
- Alterations of cortical synaptic markers in alcohol dependence
- Neurobehavioral effects of early exposure to psychotherapeutic agents
- Agmatine, neuroprotection and depression
- Role of mu-opioid system in methamphetamine sensitization
- Galanin in locus coeruleus - ventral tegmental area axons

Research Resources:
- Cellular neuroimaging core – laser-scanning confocal and light microscopes; Fuji phosphor image analysis system; Kodak imaging station; cell counting systems
- Behavioral studies core – computer-controlled operant chambers; water mazes and swim tests for rodents; locomotor activity testing equipment; digital video monitoring and motion tracking systems
- Human brain collection core – psychiatrically characterized post-mortem brain specimens
- Molecular biology core – Veritas LCM; Bio-Rad real-time PCR machine; Aligent bioanalyzer; Veritas luminometer; Bio-Rad gel doc system; NanoDrop spectrophometer; Leica cryostat.
- Website Core – homepage for programmatic descriptions and contact information for all personnel, and secure, on-line links for access to 1) scheduling of common research equipments, and 2) utilization of the Human Brain Collection Database: a secure, searchable and extensible relational database for tissue samples in the collection, which catalogues all postmortem forensic psychiatric information for individual cases

Index Terms:
psychiatric neuroscience, behavior, cognition, substance abuse, mood disorders, depression, schizophrenia, psychotherapeutic drugs, nitric oxide, agmatine, CNS development, genomics

Pesticide Toxicity to the Nervous and Endocrine Systems
Mississippi State University College of Veterinary Medicine – P20 RR017661

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http://www.msstate.edu/center/cehs/cobre/

Thematic Scientific Focus:
Environmental health, focusing on toxicological effects of pesticides on mammalian nervous and endocrine systems and links between pesticide exposures and cancer incidence

Representative Research Projects:
- Effect of organophosphate insecticides on brain development
- *In vivo* and *in vitro* effects of the pesticide atrazine on basal ganglia function
- Pesticide-induced differentiation and heterogeneity in breast cancer cells
- Epidemiology and exposure assessment of pesticides
- Biotransformation and pharmacokinetics of pyrethroid insecticides
- Molecular dynamics simulations of organophosphate inhibition of cholinesterase

Research Resources:
- Analytical instrumentation core – technical assistance with analytical and molecular techniques, instrument maintenance and training
- Biostatistics core – experimental design; data management; statistical analysis
- Animal care core – routine and specialized veterinary care; technical assistance with animal protocols; staff training in animal care procedures; biosecurity and laboratory sentinel programs

Index Terms:
environmental health, pesticide toxicity, neurotoxicity, environmental estrogens, developmental neurotoxicity, neurodegeneration, cancer, epidemiology, pesticide exposure assessment, computational chemistry, cardiovascular toxicity

back to top

Montana

Center for Environmental Health Sciences
University of Montana, Missoula – P20 RR017670

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http://www.umt.edu/cehs

Thematic Scientific Focus:
Effects of environmental agents on human health and disease, focusing on respiratory and immunotoxicology, neurotoxicology, molecular and genetic toxicology, and cardiovascular and developmental toxicology

Representative Research Projects:
- Mechanism of cardiovascular disease from arsenic exposure
- Current evaluation of Libby asbestos exposures
- Effect of lead on development of auditory temporal processing
- Biomarkers of oxidative stress following arsenic exposure
- Effect of metal mixtures on gene expression and carcinogenesis
- Response in lung extracellular matrix to asbestos

Research Resources:
- Mass spectrometry and proteomics core – LCT, QTOF, MALDI-DE, and inductively coupled plasma mass spectrometers
- Gene microarray core – robotic arrayer, scanner, expression profiling, polymorphism detection
- Fluorescence imaging core – confocal microscopes; flow cytometer and high-speed cell sorter; laser scanning cytometer with motorized stage for high-throughput scanning of microscope slide specimens; high-resolution CCD video and digital cameras
- Molecular histology core – microtomes, cryostats, staining hoods, embedding equipment
- Separations core – analytical and preparative HPLC separations of peptides and nucleic acids
- Molecular computational core – computer graphics workstations and software for modeling structure-function relationships, protein-ligand and protein-protein interactions
- Animal facility – includes surgical suites for rodents and large animals

Index Terms:
environmental health, toxicology, arsenic toxicity, lead toxicity, cardiovascular disease, oxidative stress, carcinogenesis, receptor signaling, dendritic cells

Center for Immunotherapies to Zoonotic Diseases
Montana State University – P20 RR020185

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Thematic Scientific Focus:
The pathogenesis of zoonotic diseases, and the development of immunotherapies to diseases that affect man, livestock and wildlife

Representative Research Projects:
- *Toxoplasma gondii*: the molecular basis of host-parasite communication
- Metal uptake and regulation in *Streptococcus pyogenes*
- Neutrophil function in Aspergillosis immunity
- Role of copper in prion diseases

Research Resources:
- Genomics and proteomics core – technical expertise and training for reagent development in genomics, e.g., nucleic acid isolation, genetic library construction, and probes for conventional and microarray hybridization and proteomics; computer assisted analysis of genomic and proteomic data
- Cell analysis core – flow cytometry and confocal microscopy services

Index Terms:
zoonotic diseases, infectious agents, *Toxoplasma gondii*, *Streptococcus pyogenes*, Aspergillosis, prions

Center for Structural and Functional Neuroscience
University of Montana – P20 RR015583

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http://www.umt.edu/csfn/

Thematic Scientific Focus:
Protein structure and function in the central nervous system, focusing on transport, membrane protein dynamics, and mechanisms of neurodegeneration

Representative Research Projects:
- Mapping serotonin and norepinephrine transporter binding domains
- Molecular analysis of signaling endosomes
- Glutathione: linking DNA repair regulation and neuronal vulnerability
- CNS glutamate and glutamine transport: a multidisciplinary approach

Research Resources:
- Mass spectrometry and proteomics core – Micromass LCT mass spectrometer; Micromass QTOF Micro mass spectrometer; Applied Biosystems MALDI mass spectrometer; Waters capillary liquid chromatograph; Waters HPLC 2790XE; Biorad robotic spot cutter
- Core laboratory for biospectroscopy – two ultra-fast Ti:Sapphire lasers for time-resolved spectroscopy and imaging; SPEX fluorometer; Hitachi absorption spectrometer; fluorescence microscope and scan-head for multi-photon imaging
- Molecular histology and fluorescence imaging core – includes microtomes, cryostats, auto-stainer, tissue processor, and embedding center for histology; the light/epifluor microscope with DIC optics is equipped with Nuance multispectral imaging software and the BioRad confocal microscope has three lasers for imaging
- Molecular computational core – Supercomputer arrays linked to 3D graphics workstations with software for modeling structure-function relationships, protein-ligand and protein-protein interactions
- Animal facility – AAALAC certified facility includes SPF facilities and surgical suites for rodents and large animals

Index Terms:
spectroscopy, molecular modeling, proteomics, neuroscience, central nervous system, protein structure, protein function, signaling, neurological diseases, prion diseases, depression, anxiety, obsessive-compulsive disorder, migraine, hearing

back to top

Nebraska

Center for the Molecular Biology of Neurosensory Systems
University of Nebraska Medical Center – P20 RR018788

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http://www.unmc.edu/dept/moleculargenetics/index.cfm?L2_ID=10&L1_ID=2&CONREF=8

Thematic Scientific Focus:
The molecular mechanisms that underlie neurosensory disorders, and the optimal means of intervention

Representative Research Projects:
- Test the hypotheses that epidermal growth factor receptor (EGFR) signaling is required for proper development of the peripheral nervous system (PNS) and that interactions between neural and target cells regulate PNS development
- Examine the processes involved in the repair of the central and peripheral nervous systems following virus-induced damage to the myelin of the spinal cord and sciatic nerves
- Identify and characterize the genetic/biochemical pathways regulated by microphthalmia-associated transcription factor (MITF) in development of the retinal pigment epithelium (RPE) and in the stria vascularis of the inner ear; including deducing the function of MITF in cell fate determination in the RPE and stria, its response to endothelial growth factors, and its role in modulating oxidative stress
- Demonstrate the role of OC90 in bodily balancing, in limiting otoconia formation to the inner ear, and in maintaining proper otoconia concentration

Research Resources:
- Mouse genome engineering core – expertise in the construction of transgenic and knockout mice
- Histology core – specialized morphological and histological analysis of neurosensory development; phenotyping services
- DNA microarray core – services to determine global gene expression patterns, transcriptional profiling and DNA-protein interactions

Index Terms:
neurosensory disorders, central nervous system, peripheral nervous system, epidermal growth factor receptor, nerve repair, inner ear development, balance control, otoconia

Nebraska Center for Cellular Signaling
University of Nebraska Medical Center – P20 RR018759

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Thematic Scientific Focus:
Elucidation of cellular signaling transduction mechanisms with particular emphasis on cell motility, growth regulation, apoptosis, metastasis, invasion, and cell adhesion receptors, including receptor tyrosine kinases

Representative Research Projects:
- Determine the role of the erbB2 receptor tyrosine kinase in the response of the skin to ultraviolet radiation
- Production of hyaluronan in prostate tumorigenesis
- Role of desmosomes in oral squamous cell carcinoma
- Role of recycling in integrin-mediated signaling

Research Resources:
- Microscopy core – electron and confocal laser scanning
- Histology core
- Molecular biology core
- Monoclonal antibody core
- Tissue culture core
- Flow cytometry core – Becton Dickinson FACStarPlus flow cytometer operating under Lysis II; Ortho Cytofluorograph System 50H flow cytometer operating under Cytomation software; Meridian ACAS 570 Confocal Laser Scanning Cytometer
- Microarray core
- Biostatistics core
- Human tissue bank
- Protein structure core facilities
- Animal facility
- Transgenic mouse facility

Index Terms:
signal transduction, cell adhesion, skin cancer, prostate cancer, oral cancer

Nebraska Center for Virology
University of Nebraska, Lincoln – P20 RR015635

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http://www.unl.edu/virologycenter

Thematic Scientific Focus:
Fundamental mechanisms and regulation of the replicative cycle of human viruses and host responses involved in disease pathogenesis

Representative Research Projects:
- Cellular mechanisms for HIV-1-induced neuronal injury
- Neurodegeneration and neurorestitution in murine HIV-1 encephalitis
- Inhibition of apoptosis by alphaherpesvirus latency-associated transcript
- Host cell contributions to retroviral assembly
- Herpes virus and cell interactions
- RNA virus genome replication and virus assembly
- Proteomics analysis of HIV-1-infected macrophages
- Replication of human papillomaviruses

Research Resources:
- DNA microarray core – human and mouse oligonucleotide arrays; robotic arrayer; confocal laser microarray scanner
- Microscopy core – upright and inverted confocal microscopes; laser capture microdissection system; transmission and scanning electron microscopes
- Proteomics and Genomics Core – LC/MS, ESI and MALDI mass spectrometers for protein identification and quantification
- Flow cytometry core – BSL-3 containment level fluorescence-activated cell sorter for analyzing virus-infected cells

Index Terms:
virus, pathogens, bioinformatics, microscopy, structural biology, HIV, neurodegenerative diseases, apoptosis, herpes, inflammatory disease, signaling, immunology, neuropharmacology, electrophysiology, stress, trauma, antiviral, prion diseases

Redox Biology Center
University of Nebraska, Lincoln – P20 RR017675

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http://www.unl.edu/RedoxBiologyCenter/

Thematic Scientific Focus:
Biological oxidation-reduction reactions that regulate normal cellular functions, including those that may influence the pathophysiology of human diseases linked to oxidative stress

Representative Research Projects:
- Role of cytochromes in ascorbate-linked redox homeostasis in mammalian cells
- Oxidative activation of quinones and mutagenesis
- Redox protein identification by bioinformatics
- Structure-function relationships in enzymes involved in glutathione synthesis and recovery
- Redox regulation of transcription factor activity in a plant model system
- O_2 sensing in the carotid body: in search of a membrane hemoproteic sensor that modulates K channel function
- Role of proline during oxidative stress and apoptosis
- Structure/function relationships of eukaryotic DJ-1-like proteins
- Regulation of multifunctional PutA flavoprotein & proline metabolism
- Central nervous system associations with elevated reactive oxygen species
- Oxidative stress in the androgen-independence of PCA cells
- Macromolecular crystallography: enzyme and crystallography of GSH enzymes
- Mammalian copper transport: homeostatis and its defects
- Metabolic regulation of Staphylococcal pathogenesis
- Role of ion channels in ROS production by microglia
- Structural and functional studies of DJ-1

Research Resources:
- Spectroscopy core – electron paramagnetic resonance Bruker EMX spectrometer with a continuous He cryostat model ESR 900 and the resonators ER 4102ST and ER 4119HS capable of Q-band EPR, rapid freeze quench and chemical quench apparatus, isothermal titration calorimeter, Olis RSM UV/Visible absorbance and fluorescence spectrophotometer, Olis RSM circular dichroism apparatus, applied photophysics single wavelength and diode array stopped flow spectrophotometer and spectrofluorimeter

- Metabolomics and macromolecular analysis core – ABI 4000 Qtrap (quadrupole ion trap); Q-Star XL ASBI (quadrapole-TOF) tandem mass spectrometers equipped with ESI (microspray and nanospray) and APCI sources; nano flow LC Packings UltiMate and micro flow Shimatzu HPLC systems for LC-MS or LC-MS/MS analysis of complex analytes mixtures — gel-based or in-solution proteins are digested and analyzed using LC MS/MS; proteins are identified using in-house Mascot database search; MS-based methods are available for identification and mapping of post-translational modification of proteins; facilities for analyzing low molecular weight metabolites, proteins and protein modifications and protein-protein interactions
- Microscopy core – upright and inverted confocal microscopes; laser capture microdissection system; transmission and scanning electron microscopes
- Bioinformatics core – computational resources for molecular modeling, database design and data mining, and gene sequence and expression analyses
- Genomics core – DNA microarrays; robotic arrayer; confocal laser microarray scanner

Index Terms:
redox biology, biochemistry, oxidative stress, metalloenzymes, redox signaling

back to top

Nevada

Chloride Channel Function and Role in Cardiovascular Disease
University Of Nevada, Reno – P20 RR015581

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Thematic Scientific Focus:
Role of chloride channels in normal cardiac function and disease

Representative Research Projects:
- Molecular physiology and regulation of volume sensitive chloride channels
- Signal transduction pathways regulated by cell volume
- Characterization and genomic studies of cardiovascular chloride
- Chloride channel function in animal models of cardiac disease

Research Resources:
- Targeted and transgenic mouse core – animal breeding and maintenance facility; ES cell culture and gene targeting services (null, tissue-specific, and inducible knock-out gene constructs); microinjection expertise and equipment for blastocyst and pronuclear injections; strain cryopreservation and rederivation via IVF and embryo transfer; mouse genotyping
- Imaging core – immuno- and enzyme histochemical staining techniques for protein localization in tissues and cells, including subcellular co-localization and reorganization; upright histology microscope; transmission electron microscope; inverted fluorescent microscope; confocal microscope; digital camera imaging system; cryostat
- Molecular and genomics core – expression vector constructs; promoter mapping; custom BAC and YAC analyses

Index Terms:
transgenic animals, molecular biology, genomics, imaging, cardiovascular disease, electrophysiology, genetics, cystic fibrosis, myotonia, kidney disease, cardiac arrhythmia, congestive heart failure

Smooth Muscle Plasticity: A COBRE
University of Nevada School of Medicine – P20RR018751

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Thematic Scientific Focus:
The causes and consequences of the ability of smooth muscles to change phenotype to conform to changing stimuli or microenvironments

Research Projects:
- Understand the functional roles of the 7 1-integrin in regulating vascular smooth muscle plasticity and in vascular disease
- Elucidate the physiological significance of the tissue-specific expression of the subunit isoforms ( ) comprising the multifunctional Ca^{2+}/calmodulin-dependent protein kinase II (CaMKII)
- Examine the physiological changes that occur during obstructive bowel disease; specifically, analyze the hypertrophic changes in the neuronal circuits and chemical coding of specific classes of enteric neurons
- Characterize stretch-dependent potassium channels (SDK) in the bladder to understand the physiological basis for filling mechanisms and pathological distension

Research Resources:
- Molecular expression and transgenic core – coordinates the procurement and maintenance of mouse transgenic lines; provides adenoviral gene transfer vectors and protein transduction reagents; assesses mRNA and protein expression for all projects by RT-PCR and western blotting
- Cell proteomics interface facility – provides computational expertise in analyzing protein structures and experimental expertise in the isolation, purification and subsequent analysis of proteins, including mass spectrometry
- Dynamic imaging facility – provides expertise in fluorescent imaging; employs a high speed fluorescent imaging system and a ratio metric (Fura 2-AM) imaging system for use with pressurized blood vessels and isolated cells

Index Terms:
smooth muscle biology, smooth muscle plasticity, integrins, calmodulin, smooth muscle proteomics, stretch-activated potassium channels, bowel obstructions

back to top

New Hampshire

Cellular and Molecular Mechanisms of Lung Disease
Dartmouth Medical School – P20 RR018787

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Thematic Scientific Focus:
The molecular and cellular mechanisms that underlie the initiation, pathogenesis, progression and treatment of lung disease

Representative Research Projects:
- Environmental epidemiology of lung cancer in New Hampshire
- Structural analysis of CFTR proteins interaction.
- Regulation of biofilm development on epithelial cells
- Regulation of endocytic trafficking of CFTR
- Respiratory effects of airborne particulate matter

Research Resources:
- Proteomics core – a complete array of protein analysis services, including access to a Biacore X SPR biosensor to perform surface plasmon resonance studies (SPR)

Index Terms:
lung cancer, cystic fibrosis, Pseudomonas aeruginosa, cystic fibrosis transmembrane conductance regulator, biofilm, environmenatl epidemiology

Center for Molecular, Cellular, and Translational Immunological Research
Dartmouth Medical School – P20 RR016437

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Thematic Scientific Focus:
Modulation of immunity in various disease states, via non-specific and antigen-specific immune response pathways, to find new ways to influence immune responses to combat tumors and bacterial infections, or to suppress inflammation and autoimmunity

Representative Research Projects:
- Stat5: Role in Cytotoxic T-cell Development and Oncogenesis
- Scavenger receptor function in chaperone-elicited adaptive immune responses
- Vascular Leukocytes: Basic Immunobiology and Functional Plasticity
- Role of the chromatin regulator, MLL, in T cell development

Research Resources:
- Molecular biology core – custom production of biologic and immunogenic reagents; cytokine and chemokine analysis
- Transgenic mice core – general animal husbandry; custom production of transgenic DNA constructs and mice; mouse breeding and genotyping; strain preservation and rederivation

Index Terms:
cancer, inflammation, immunology, infection

back to top

New Mexico

Center for Evolutionary and Theoretical Immunology
University of New Mexico – P20 RR018754

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Thematic Scientific Focus
Dedicated to studying the origins, evolution and diversification of immune systems and to understand from a theoretical point of view the principles that underlie defense systems.

Representative Research Projects:
- The maintenance of fetal maternal tolerance in marsupials
- The spontaneous rate of gene duplication and deletion
- Mathematical modeling of signal transduction by a TIR receptor
- Computational quantitative modeling of RNA interference
- Modeling of immune responses in infectious diseases
- Diverse recognition capability: an invertebrate model
- Expression profiling of defense and stress related genes of *Schistosoma mansoni*

Research Resources:
- Molecular Biology Facility – two ABI 3100 DNA Sequencers; ABI 377 DNA Sequencer; NanoDrop ND-1000 Spectrophotometer; Kodak Gel Logic 200 Digital Imaging System; ABI 7000 Q-PCR; MJ Research Tetrad thermocycler; Beckman L-70 Ultra-Centrifuge; Kodak Image Station 440
- Controlled Environment Facility – two Conviron E8 reach-in environmental chambers and one Conviron C1006 controlled environment room; a fully equipped tissue culture room
- Mass Spectrometry Facility – ABI 4700 MALDI Tof-Tof mass spectrometer; Waters LCT premier ESI-Tof mass spectrometer; Finnigan TSQ-7000 mass spectrometer

Index Terms:
evolutionary immunobiology, theoretical immunology, innate immunity, immunology, RNAi, comparative immunology, evolution, host-pathogen interaction

Integrative Program in CNS Pathophysiology Research
University Of New Mexico – P20 RR015636

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Thematic Scientific Focus:
Integrative, multimodal neuroimaging research focused on the pathophysiology of ischemic stroke, hemorrhagic stroke, traumatic brain injury, and epilepsy

Representative Research Projects:
- Mechanisms of ischemic brain injury mediated by free radicals
- Mechanisms of delayed cell death following injury to the central nervous system
- Characterization of intracerebral hemorrhage in a piglet brain model system
- Generators of human frontal lobe epilepsy

Research Resources:
- Magnetic resonance imaging core – Bruker 4.7T actively shielded scanner with 40 cm bore for non-invasive large and small animal studies
- Electron paramagnetic resonance core – Bruker EPR spectrometer and *in vivo* imager for analytical studies and *in vivo* non-invasive imaging of reactive oxygen species
- Magneto- and electroencephalography core – high-resolution MEG systems (microSQUID and 64-channel EEG systems) for non-invasive monitoring of brain electrophysiological activities
- Optical imaging core – 2-photon scanning laser microscope; photodiode array; DIC infrared microscopy; *in vivo* and *in vitro* imaging of membrane potentials and intracellular calcium
- Cellular and molecular biology core – RT-PCR; microplate reader; fluorescence microscopes; immunohistochemistry for degeneration, regeneration, and inflammation studies

Index Terms:
magnetoencephalography, magnetic resonance, electron paramagnetic resonance, optical imaging, cell biology, molecular biology, central nervous system injury, pathophysiology, inflammation, ischemia, intracerebral hemorrhage, electrophysiology, stroke, epilepsy

back to top

North Dakota

Center for Visual Neuroscience
North Dakota State University – P20 RR020151

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Thematic Scientific Focus:
Analyzing visual performance in normal and dysfunctional states, to develop clinically useful diagnostic tests for assessing visual performance, to understand the neural mechanisms that control eye movements under natural environmental conditions, to understand how the brain processes visual information, how neural activity is related to visual perception, and how visual processing interacts with other brain systems which underlie cognition and action

Representative Research Projects:
- Attention and the representation of visual environments
- Inhibition and age-related changes in visual search
- Visual orienting effects of directional cues
- Mechanisms of object recognition
- Mechanisms of visual grouping
- Mechanisms of multisensory sensory interaction and attention

Research Resources:
- High-density electroencephalography core laboratory – supports functional neuroimaging approaches to the scientific themes of the center projects; twin state-of-the-art 168-channel EEG data acquisition and analysis systems housed in electromagnetically-shielded recording chambers; gigabit intranet connectivity with a terabyte data storage array and several high-performance EEG analysis workstations

Index Terms:
visual processing, eye control, visual neural activity, cognition

Center for Protease Research
North Dakota State University – P20 RR015566

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Thematic Scientific Focus:
Novel strategies for targeting human diseases through protease inhibition, starting with *in vitro* cellular interactions and continuing through stages of lead product synthesis to drug design and delivery

Representative Research Projects:
- Synthesis of inhibitors of matrix metalloproteinases, serine proteases, urokinase and plasmin
- Targeting and delivery of matrix metalloproteinase inhibitors
- Biopharmaceuticals: computational methods and quantitative structure-time-activity relationships

Research Resources:
- Mass spectral facility – Bio-TOF III high resolution mass spectrometer and Esquire 3000 MS/MS system
- Microscopy facility – confocal microscope

Index Terms:
drug design, cancer, drug delivery, arthritis, multiple sclerosis, osteoporosis, Alzheimer's disease

COBRE in Pathophysiology of Neurodegenerative Disease
University of North Dakota School of Medicine & Health Sciences – P20 RR017699

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Thematic Scientific Focus:
Cellular mechanisms that contribute to neuronal degeneration and chronic neurodegenerative diseases

Representative Research Projects:
- TNF-alpha/glutamate-induced cell death in Alzheimer's disease
- Cellular mechanisms of substance P in epilepsy
- Carbonyl detoxification in the central nervous system
- Alpha-Synuclein in brain lipid metabolism
- Adrenergic modulation of seizures and neurodegeneration

Research Resources:
- Mass spectrometry core – high-resolution electrospray-quadrupole/time-of-flight MS, electrospray-triple quadrupole MS, and gas chromatography-ion trap MS
- Imaging core – Hitachi transmission and scanning electron microscopes; Olympus FluoView 300 laser scanning confocal microscope; Zeiss 510 Meta confocal microscope (seven fluorescent channels, one DIC channel); ConfoCor2 fluorescence correlation spectroscopy unit; Axiovert200 microscope with AxioCam HRM digital camera; computer workstation and software for image data processing and analysis

Index Terms:
neurodegeneration, Alzheimer's disease, inflammation, necrosis, apoptosis, cytokines, calcitonin, carbonyl detoxification, phospholipid metabolism, a-synuclein, epilepsy

back to top

Oklahoma

Biofilm Formation and Metabolism on Dental Surfaces
University of Oklahoma Health Sciences Center – P20 RR018741

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Thematic Scientific Focus:
Microbial biofilm formation and metabolism on natural and artificial dental surfaces

Representative Research Projects:
- Further develop an understanding of how clinically relevant biofilm forming bacteria influence the behavior and metabolism of host tissue cells
- Investigate the effect of dental restorative treatments on biofilm accumulation
- Analyze the differences on global gene expression of *Streptococcus mutans* exposed to different dietary sugars to gather information on how gene expression patterns vary under sessile or planktonic conditions
- Identify the processes needed for attachment and biofilm formation in *Actinobacillus actinomycetemcomitans* and evaluate their impact on pathogenesis and persistence in the oral cavity

Research Resources:
- Microscopy core facility – Leica TCS NT confocal microscope
- Microarray facility – GeneTAC Microarray analyzer; ABI Real-Time PCR 7000 Sequence detection system
- Genomics Core and Training facility – fully equipped Affymetrix GeneChip technology

Index Terms:
Biofilms, periodontal disease, gingivitis, dental caries, dental surfaces

Functional Genomic/Proteomic Analysis of Bacterial/Host Interactions
University of Oklahoma Health Sciences Center – P20 RR015564

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http://w3.ouhsc.edu/mi/assets/COBRE.htm.ppt (site under construction)

Thematic Scientific Focus:
Genome-scale analysis of bacterial pathogenesis, emphasizing functional genomic and proteomic analysis of bacteria-host interactions

Representative Research Projects:
- Functional genomic and proteomic analysis of *Campylobacter*
- Functional genomics and proteomics of *Bacillus anthracis*
- Functional genomic and proteomic analysis of *Borrelia burgdorferi*
- Global gene expression in *Staphylococcus aureus*
- Gene expression in *Pseudomonas aeruginosa* biofilms

Research Resources:
- Functional genomics cores (OUHSC and OSU) – microarray fabrication, hybridization, and scanning; microarray-based gene expression profiling; high-throughput DNA sequencing and oligonucleotide synthesis; protein 2-D gel electrophoresis and N-terminal amino acid sequencing
- Informatics core – computer hardware and software for primer design, image processing, and data analysis

Index Terms:
genomics, proteomics, DNA microarray, bacteria, pathogens, Lyme disease, *E. coli*, enteritis, *Campylobacter*, anthrax, food poisoning

Mentoring Vision Research in Oklahoma
University of Oklahoma Health Sciences Center – P20 RR017703

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Thematic Scientific Focus:
Basic visual research with an emphasis on studying the retina and retinal diseases

Representative Research Projects:
- Regulation of vascular development in mouse retina
- Photoreceptor protection in tubby mouse, a phenotypic animal model for Usher syndrome
- HIF-1 as therapeutic target in diabetic retinopathy
- Role of PI 3-kinase and its downstream target Bcl-xL in retinal pigment epithelial cells
- Insulin receptor signaling in retina
- Wnt signaling and retinal regulation of circadian rhythmicity
- *In vivo* role of caveolin-1 in knockout and transgenic mouse retinas
- Photoreceptor retinol dehydrogenases and vision
- Biochemical and functional characterization of the cone CNG channel

Research Resources:
- Proteomics/bioinformatics core
- Image acquisition and production core
- Microinjection core
- Microarray core
- Molecular biology core
- Animal Resource Module – animal surgery, antibody production, and electroretinography

Index Terms:
visual research, retinal disease, retinal biochemistry, light-induced signal transduction, neurodegeneration, diabetes, angiogenesis, vascularization

Mentoring Immunology in Oklahoma: A Biomedical Program
Oklahoma Medical Research Foundation – P20 RR015577

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http://www.omrf.ouhsc.edu/OMRF/Information/IDeA/IDeAGrant.asp

Thematic Scientific Focus:
Molecular and cellular immunology in the context of human health and disease

Representative Research Projects:
- Human gamma herpes virus DNA vaccines
- Role of bHLH proteins in human lymphopoiesis
- Neutrophil phenotyping in periodic and chronic arthritis
- Stat1 in IL-6-mediated T cell homeostasis
- B cell tolerance during secondary immune responses

Research Resources:
- Microarray core – Printing of mouse and human genome-scale arrays; high-throughput Ventana hybridization station; microarray processing and image analysis; data warehousing; bioinformatics and statistical analyses
- Signal transduction core – measurements of intracellular calcium, protein-protein interactions, enzyme activities; phosphoaminoacid analysis; Perkin-Elmer LS-50 spectrofluorimeter; Roche Lumi-imager for immuno-detection and quantification of proteins and nucleic acids on filters; BioRad medium-pressure chromatography system; Hunter thin layer electrophoresis apparatus; Molecular Dynamics Storm System for radiolabel quantification; transient transfection services
- Imaging core – Hitachi H-7600 transmission electron microscope; Zeiss Axiovert 200 inverted fluorescence microscope; Zeiss Axiostar upright microscope
- Peptide synthesis core – custom synthetic peptides for biochemical studies and solid-phase peptide epitope mapping experiments
- Microinjection core – production of transgenic and gene-targeted mice by zygote injection and injection of embryonic stem cells into blastocysts; rederivation of mouse strains; two inverted microscopes with Hoffman DIC and phase contrast optics, fitted with Narishige fine- and coarse micromanipulators for embryo manipulation and a cooling stage for ES cells injections; three surgical microscopes (Nikon SMZ-2T, Nikon SMZ-U); deFonbrune microforge; Sutter P-97 pipette puller; laminar flow cell culture hood; CO2 incubator; inverted light microscope

Index Terms:
immunology, molecular biology, vaccine, drug design, herpes, virus, signaling, inflammation, inflammatory disease, DNA microarray, imaging, proteomics, microinjection, stem cells, immunodeficiency, autoimmune disease, arthritis, genomics

Molecular Mechanisms and Genetics of Autoimmunity
Oklahoma Medical Research Foundation – P20 RR020143

Principal Investigator:
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http://www.omrf.org/OMRF/Research/09/Welcome.asp

Thematic Scientific Focus:
The molecular and genetic basis for autoimmune diseases

Representative Research Projects:
- Genetic association in pediatric patients with systemic lupus erythematosus (SLE)
- Neutrophil proteinase-3 autoantigen expression and regulation
- Genetics of B lymphocyte signaling in Lupus
- Whole genome admixture mapping for SLE

Research Resources:
- Nucleic acid analysis core – sequencing, genotyping, oligonucleotide synthesis, custom expression arrays; Biotage Rotor-Gene 3000 four-channel multiplexing system; Affymetrix 3000 genechip scanner system with autoloader
- Data analysis core – statistical and bioinformatic analyses

Index Terms:
autoimmune disease, inflammatory rheumatic diseases, systemic lupus erythematosus, autoantibody, autoantigen

Post-Translational Modifications in Host Defense
Oklahoma Medical Research Foundation – P20 RR018758

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Thematic Scientific Focus:
The role of glycosylation in host defense

Representative Research Projects:
- How membrane tether formation stabilizes leukocyte rolling, thus enabling leukocytes to survey the endothelium for mediators of inflammation
- The role of VH4-34 immunoglobulin heavy chain gene encoded antibody immunity and the mechanisms that provide natural immunity while avoiding an autoimmune response
- The mechanisms by which TFPI interacts with membrane surfaces
- The role of O-glycosylation in development, inflammation, hemostasis, immune responses, and other biological functions *in vivo*
- The role of proteoglycans, specifically chondroitin sulfate and dermatan sulfate, biosynthesis in atherogenesis

Research Resources:
- *In vitro* microscopy core – provides expertise and the equipment to perform a diversity of techniques that include brightfield histological analysis, confocal microscopy, 3D imaging, standard transmission electron microscopy and immunogold labeling, and advanced cryo-technologies (cryoimmunogold labeling, freeze substitution, high pressure freezing, and freeze fracture and deep-etching)
- Intravital microscope core – provides expertise and equipment to dissect complex physiological or pathological cell-cell or cell-matrix interactions; advanced Nikon ECLIPSE E600-FN intravital epifluorescence microscope with water immersion objectives connected to a Dage-MTI DC-330 3CCD color camera, a SVHS video cassette recorder, and a Microvessel Velocity OD-RT Doppler apparatus; Nikon SMZ800 stereo microscope for surgical preparation; advanced Dell computer for data acquisition and analysis
- MRI/MRS core – provides non-invasive in vivo monitoring capabilities to assess morphological, physiological, pathophysiological and metabolic processes that occur during progressive stages of the pathogenesis of most diseases

Index Terms:
host defense, inflammation, antibody, autoimmune disease, immunoglobulins, glycosylation, proteoglycans, atherogenesis

back to top

Puerto Rico

Center for Molecular, Developmental and Behavioral Neuroscience
University of Puerto Rico Medical Sciences – P20 RR015565

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Thematic Scientific Focus:
Molecular mechanisms underlying neuronal injury, emotional memory, cocaine-seeking behavior, and the expression of maternal behavior

Representative Research Projects:
- P2Y2 nucleotide receptor in ischemia
- Genomic basis of emotional learning and memory
- Neuropeptide modulation and gene expression in cocaine seeking behavior
- Neurosteroid effects in the structure and function of a sexually dimorphic network

Research Resources:
- Research core – DNA microarray instrumentation.

Index Terms:
DNA microarray, neuroscience, stroke, ischemia, neuronal injury, molecular biology, schizophrenia, anxiety, memory, genomics, proteomics, drug abuse, endocrinology

UPR Protein Research Center
University of Puerto Rico, Mayaguez – P20 RR016439

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Thematic Scientific Focus:
Fundamental protein chemistry, proteomics and genomics, using x-ray diffraction, proteomic mass spectrometry, and computational techniques

Representative Research Projects:
- Biophysics of unusual hemoglobins that show functions other than reversible oxygen binding
- The correlation between biophysical structure of an enzyme and its function
- Protein structure and function in unusual chemical settings (drug delivery systems)

Research Resources:
- Computational facilities – capable of protein dynamics simulations
- X-ray crystallography facilities
- Proteomic mass spectrometry facilities
- FT-IR/RAMAN facilities
- Light scattering facilities
- Circular dichroism (CD) facilities
- Transient kinetics: flash photolysis, stopped-flow spectrophotometry

Index Terms:
proteomics, genomics, protein chemistry, protein structure, protein function, enzymology, proteomic mass spectrometry, x-ray diffraction, biophysics, drug delivery

back to top

Rhode Island

Center for Cancer Research Development
Rhode Island Hospital – P20 RR017695

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http://www.rih-cobre-cares.org/index.html

Thematic Scientific Focus:
Molecular targets for cancer intervention

Representative Research Projects:
- Biomarkers for predicting response to therapy, prognosis, staging
- Targets for molecular intervention using siRNA, specific inhibitors
- Targeting signaling pathways that increase sensitivity to conventional treatments
- Molecular pathways targeted by environmental, physiological, or infectious agents

Research Resources:
- Proteomics Core – makes state-of-the-art protein and analysis/purification instrumentation and techniques available for specific research projects; assists investigators in choosing appropriate methods and techniques for specific research objectives; provides a means for investigators to become directly involved in protein analysis at a level not possible with commercial suppliers; provides expertise in protein bioinformatics
- Molecular Pathology Core – provides instrumentation and support personnel for the research efforts of both the COBRE mentors and their junior associates, as well as specialty immunohistochemical services for the Department of Pathology; 1250 ft^2 facility is equipped with an Arcturus AutoPix automated laser capture microdissection instrument, Olympus BX41 with CoolSnap Camera from Media Cybernetics and Image Pro-Plus Software, Stratagene MX4000 quantitative real-time PCR system, BioRad iCycler, Agilent BioAnalyser, Ventana Discovery automated immunohistochemistry processor, microtome and cryostat, Beecher tissue arrayer, and 40 ft^3 of -80°C freezer space for the tumor bank

Index Terms:
cancer, hepatocarcinoma, vaccines, colon cancer, esophageal cancer, liver cancer, anti-inflammatory cytokines, *Helicobacter pylori*, gastric cancer, liver development, signal transduction

Center for Genomics and Proteomics
Brown University – P20 RR015578

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http://www.brown.edu/Research/CGP/

Thematic Scientific Focus:
Become part of a master plan to establish a center for contemporary molecular genetics research, using a multidisciplinary approach that will combine laboratory research with clinical and human genetics at affiliated hospitals

Representative Research Projects:
- Gonad-specific transcriptional cofactors
- Wnt signaling in hepatocellular carcinoma
- High-throughput proteomic analysis of signaling pathways
- Functional studies of E3 ubiquitin ligase
- Genetic damage by lipid peroxidation
- Supv3L1 helicase knockout mouse
- Bayesian inferences of cis-regulatory modules and signal transduction pathways

Research Resources:
- Transgenic and knockout mouse facility
- Flow cytometry core
- Confocal imaging core

Index Terms:
transgenic animals, knockout mouse, flow cytometry, imaging, genetics, genomics, immunology, infection, molecular biology, virus, hepatitis, neuropathology, Alzheimer's disease, microvascular disease, addiction, epilepsy, stroke, signaling, liver disease

COBRE for Perinatal Biology
Women & Infants' Hospital of Rhode Island – P20 RR018728

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http://bms.brown.edu/COBRE/

Thematic Scientific Focus:
The molecular basis of cardiopulmonary signal transduction and development during fetal and postnatal life

Representative Research Projects:
- Determine the role of the cell cycle inhibitor p57KIP2 in ventricular myocyte differentiation
- Elucidate the signaling pathways that regulate cardiomyocyte proliferation
- Identify the mechanotransduction mechanisms that regulate lung alveolar differentiation
- Define the role of Fas-mediated apoptosis in perinatal lung remodeling

Research Resources:
- Molecular biology and histology core – radiographic imaging, multifluorescent imaging, tissue processing and microscopy, including phase contrast, DIC, and fluorescence

Index Terms:
fetal development, perinatal development, cardiac development, pulmonary development, newborn medicine, signal transduction, placental development

The New Stem Cell Biology
Roger Williams Hospital – P20 RR018757

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http://www.rwmc.org/index.htm

Thematic Scientific Focus:
The regulation of proliferation and the potential for hematopoietic stem cells to differentiate into other cell types and tissues

Representative Research Projects:
- The dynamics of homing and recruitment of bone marrow stem cells to the skin to assist in wound healing
- The specifics of muscle injury which leads to high-level conversion of bone marrow stem cells to muscle cells; in addition, the particular cell type that gives rise to muscle at the highest frequency, the timing of transplant suitable for such conversions, and the number of cells necessary to obtain significant muscle conversion
- Techniques to apply RNAi technology to hematopoietic stem cells to down-regulate key transcription factors in their differentiation, thereby providing a tool to manipulate their gene expression and ultimately, their clinical application
- The basics of conversion of marrow cells to lung cells
- Studies of the regulation of hematopoiesis on a continuum and its relationship to cell cycle

Research Resources:
- Cell sorter/flow cytometry core – BD FACS scan, BD FACS calibur, and MoFLo high speed cell sorter from Cytomation
- Cell phenotyping core – two new Zeiss fluorescent motor-driven microscopes; an upright Axioplan 2, an inverted Axiovert 200M, and a Zeiss 510 confocal laser-scanning microscope capable of four-color imaging

Index Terms:
adult stem cells, hematopoietic stem cells, bone marrow, wound healing, differentiation, RNAi

back to top

South Carolina

Center for Colon Cancer Research
University of South Carolina – P20 RR017698

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Thematic Scientific Focus:
Molecular, biochemical, genetic, and lifestyle factors that affect colorectal cancer and its treatment

Representative Research Projects:
- The influence of alterations in specific cytoskeletal components on the cancerous state
- The impact of perturbations in specific DNA damage response pathways on colorectal cancer
- Whether adjuvant nutrition can increase the efficacy of colon cancer chemotherapy
- How alterations in physical activity and diet affect the expression of specific proteins that, in turn, can alter cellular processes that ultimately modify the risk of colon cancer

Research Resources:
- Animal/mouse core
- Histology/imaging core
- Pathology core – pathologic tissue diagnosis with detailed description, image illustration, and pathologic consulting for immunohistochemistry, digital quantitation, tissue microarray analysis, and tissue microdissection
- Biometry core – statistical support and new statistical methods

Index Terms:
colon cancer, cell biology, DNA repair, apoptosis, inflammation, cellular proliferation, chemotherapy, chemoprevention, nutrition, epidemiology

COBRE in Lipidomics and Pathobiology
Medical University of South Carolina – P20 RR017677

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http://biochemistry.musc.edu/cobre/

Thematic Scientific Focus:
How bioactive lipids influence cellular regulatory pathways and how specific lipids affect these control networks, which subsequently can contribute to the pathophysiology of certain disease states

Representative Research Projects:
- Role and function of mammalian sphingomyelin synthases
- Role of sphingosine kinase 1/sphingisine-1-phosphate pathway in colon carcinogenesis
- Protection of steatotic livers from primary nonfunction
- Sphingolipids in integrin-mediated oligodendrocyte survival signaling in hypoxia/ischemia
- ATP-binding cassette transporter 2 (ABCA2) regulation of betaAPP processing
- Sphingolipid signaling induced by LDL immune complexes

Research Resources:
- Lipidomics core
- Animal pathobiology core – mouse knock-out and transgenic technology for gene targeting by homologous recombination and random integration, respectively through pronuclear injections; founder mice are generated by either approach and subsequently serve as an animal resource for breeding and genotyping; rabbit model for fungal pathogenesis is being established.
- Protein science core

Index Terms:
lipids, angiogenesis, tumor progression, neuroblastoma, diabetes, fungal pathogenesis

South Carolina COBRE for Cardiovascular Disease
Medical University of South Carolina – P20 RR016434

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http://cba.musc.edu/COBRE/index.htm

Thematic Scientific Focus:
Mechanisms of cardiovascular disease, including cell proliferation and remodeling, apoptosis, cellular transdifferentiation, and vasculogenesis

Representative Research Projects:
- Transcriptional control of cardiac growth
- Role of hyaluronan in congenital heart defects and atherosclerosis
- Hematopoietic stem cells in cardiovascular regenerative medicine
- Molecular development and pathophysiology of the atrio-ventricular conduction system

Research Resources:
- Transgenic mice core
- Imaging core
- DNA microarray core
- Proteomics core

Index Terms:
cardiovascular disease, proteomics, genomics, apoptosis, cell biology, DNA microarray

South Carolina COBRE for Oral Health
Medical University of South Carolina – P20 RR017696

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http://oralcobre.musc.edu/

Thematic Scientific Focus:
Oral and craniofacial health

Representative Research Projects:
- Epidemiology of oral disease and diabetes: cytokine genes and inflammation
- Oral health in African American adolescents with diabetes in rural areas
- *Candida albicans*-associated oral biofilms
- Metastasis-associated proteins in oral and head and neck cancer
- Role of the extracellular matrix in oral cancer
- Oral cancer prevention by dietary flavonoids: role of salivary beta-glucosidase

Research Resources:
- Biostatistics core – collaboration in study design; sample size estimation and power analyses; statistical methodology, especially for clustered data; data management, including web-based systems; manuscript and proposal preparation; bioinformatics methods for proteomics research
- Clinical resources core – coordination of clinical research projects at the MUSC GCRC Research Center and at off site locations; provision of calibrated dental examiners for oral exams; coordination of research methodologies available in the MUSC Center for Oral Health Research Core Laboratory (including genotype analysis, laser scanning cytometry, and SearchLight proteome multiplex ELISA arrays)

Index Terms:
oral health, periodontal disease, cytokines, diabetes, oral cancer, genetic polymorphisms, health disparities, health education intervention

back to top

South Dakota

Mechanisms of Cardiovascular Remodeling
University of South Dakota School of Medicine – P20 RR017662

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Thematic Scientific Focus:
Multi-disciplinary, highly integrated, approach toward understanding cardiovascular disease

Representative Research Projects:
- Ubiquitin-proteasome in cardiac remodeling and failure
- Myocyte polarity and signal transduction in myocardial infarction
- P21-activated kinase (Pak) signaling in hypertrophy and heart failure
- Effect of long-term exercise on SHHF rats
- The CNS and heart failure

Research Resources:
- Physiology testing core
- Cell culture core
- Molecular biology core
- Cell imaging core

Index Terms:
cardiovascular disease, heart failure, remodeling, signal transduction, ubiquitin, myocyte polarity, cytokines

COBRE on Neural Mechanisms of Adaptive Behavior
University of South Dakota – P20 RR015567

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http://www.usd.edu/neurogroup/COBRE.cfm

Thematic Scientific Focus:
Structural reorganization in neural pathways resulting in adaptive behavioral responses to novel sensorimotor experiences; employing physiological, pharmacological, anatomical, molecular, and behavioral experimental approaches

Representative Research Projects:
- Synaptic mechanisms underlying *in vitro* classical conditioning
- Adaptation of respiratory pattern generator to hypoxia
- Steroid and monoamine effects on sex, stress and seizures
- Mechanisms underlying focal cranial cervical dystonia
- Enhanced learning and memory performance with increased neurogenesis
- Amygdala-cortical circuitry underlying stress responses in rats
- Receptor hypofunction and cellular integrity
- Viral-mediated RNA interference in the adult rat brain
- Cellular mechanisms of intrinsic and extrinsic sensitization
- Role for syngap in synaptic signaling and excitotoxicity
- Cadherins in the neural crest

Research Resources:
- Biological Imaging core – Olympus FluoView 500 Laser Scanning Confocal Microscope; Zeiss Axiovert 200 MOT inverted and Axio Imager M1 upright fluorescent microscopes
- Behavioral Core – Noldus Ethovision video tracking system; ObserverXT data analysis system; watermaze, elevated plus maze, 8 arm radial maze

Index Terms:
microscopy, conditioning, learning, memory, neurogenesis, stress, seizures, steroids, physiology, pharmacology, anatomy, behavior, molecular biology

back to top

Vermont

Neuroscience Center of Biological Research Excellence
University of Vermont – P20 RR016435

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Thematic Scientific Focus:
The molecular basis of neurological functions

Representative Research Projects:
- Chloride homeostasis in olfactory neurons
- Molecular and genetic analysis of learned fear reduction in mice
- Kinase and cytoskeletal regulation of potassium channels
- Proteolytic modulation of notch signaling in neurogenesis
- Mechanisms of cerebral vasospasm in subarachnoid hemorrhage
- Spatial regulation of protein kinase A signaling during growth cone guidance
- Expression of the AMPA receptor subunit GluR2 in chick lumbar motoneurons
- Adult bone marrow stem cells for CNS repair
- Role of dipeptidyl peptidase IV (DPPIV) in peripheral neurogenesis and neuroblastomas

Research Resources:
- Imaging and physiology core – Noran laser scanning confocal microscope; DeltaVision Restoration Microscopy System; BioRad Radiance dedicated multiphoton confocal microscope
- Cellular and molecular biology core – Molecular Dynamics STORM fluorescence and phosphoimager; LI-COR Odyssey infrared imaging system; Zeiss fluorescence microscope with Kodak MDS290 imaging system

Index Terms:
neuroscience, cell biology, molecular biology, learning, signaling, brain, vascular biology

Translational Research in Lung Biology and Disease
University of Vermont & State Agricultural College – P20 RR015557

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Thematic Scientific Focus:
Translating basic laboratory research into clinical applications to fight lung disease, while creating a stimulating research environment for promising new investigators

Representative Research Projects:
- Airway epithelial signaling cascades evoked by nitrogen dioxide
- Airway parenchymal mechanical dysfunction in asthma
- Role of altered pulmonary proteolysis in pathogenesis of asthma
- Th2 mediated airway inflammation in the delta-f508 mouse

Research Resources:
- Transgenic animal core
- Biomedical engineering core

Index Terms:
physiology, lungs, asthma, biomedical engineering, transgenic animals, signaling, inflammation

back to top

West Virginia

COBRE for Signal Transduction and Cancer
West Virginia University – P20 RR016440

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Thematic Scientific Focus:
Molecular changes in cell signaling proteins that occur in cancer; the relationship between cancer cell growth, metastasis, and signal transduction, using proteomics

Representative Research Projects:
- SHP2-mediated cross talk between the EGFr/HER2 and WNT Signaling
- A novel computational model system for constructing molecular classifiers of human cancers
- A novel tumor suppressor gene
- Role of cortactin in head and neck cancer
- Caveolin polarity and endothelial cell migration
- VE-cadherin trafficking and angiogenesis

Research Resources:
- Flow cytometry core
- Mass spectrometry core

Index Terms:
cell biology, molecular biology, proteomics, cancer, signaling, angiogenesis

COBRE in Sensory Neuroscience
West Virginia University – P20 RR015574

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Thematic Scientific Focus:
Neuroscience, focused on the topics of development and plasticity; development of treatments for human neurological diseases using both animal and human subjects

Representative Research Projects:
- Interneurons mediating feedforward thalamocortical inhibition
- Spatio-temporal coding of odor
- FMRI of auditory attention to complex environmental sounds
- Functional convergence in visual cortex
- Regulation of intracellular transducin homeostasis by phosducin in vertebrate rods

Research Resources:
- Histobiology core
- Center for Advanced Imaging
- Imaging core
- Transgenic animal core
- Proteomics and mass spectrometry core
- Computational chemistry and molecular modeling research laboratory
- Pathology and histology services
- FACS/cell sorting facility
  - Molecular biology core (Affymetrix genechip reader)

Index Terms:
neuroscience, neurons, genetics, imaging, sensory disorders, hearing, balance, signaling, molecular degeneration

Transcription Factors in Cancer
Marshall University – P20 RR020180

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Thematic Scientific Focus:
The role of transcription factors in promoting cancer, with an emphasis on the function of retinoids or their signaling pathways as a unifying focus

Representative Research Projects:
- β-catenin function and retinoic acid in melanoma
- Retinoids, NF-κβ and superoxide dismutase in neuroblastoma
- Sap, a potential zebrafish oncogene
- Ski and Sno transcription factors in testicular cancers

Research Resources:
- Imaging core – laser scanning confocal microscopy, with capability for microinjection and micromanipulation; sophisticated image analysis programs with a dedicated computer workstation; transmission electron microscopy to confirm cellular apoptosis; and laser capture microdissection for isolating normal and cancer cells from histological specimens
- Genomic core – microarray profiling; single mRNA measurement abundance by real-time PCR; DNA sequencing and sequence analysis

Index Terms:
retinoids, transcription factors, cancer

back to top

Wyoming

Biology of Spatiotemporal Nitric Oxide Gradients
University of Wyoming – P20 RR015553

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Thematic Scientific Focus:
The role of nitrous oxide (NO) concentrations and gradients as signals and as protective or damaging factors in the progression of human disease, including topics related to neurogenesis and neurodegeneration

Representative Research Projects:
- GNRH and its role in sexual behavior
- Factors controlling stimulated endothelial cell motility
- Biomimetic modeling of the fly visual system
- Adaptation to high altitude diving in river otters: Implications for human healing
- Brain microcircuits in developmental cortical malformations and epilepsy

Research Resources:
- Microscopy core – upright and inverted confocal microscopes; transmission and scanning microscopes; high quality conventional light and fluorescence microscopy equipment
- Macromolecular core – MALDI-TOF; spectrofluorometer; nitric oxide analyzer; real-time-PCR; gel reader

Index Terms:
signaling, nitrous oxide, pathology, bacteria, retrovirus, neurobiology, cell imaging, molecular biology, electrophysiology, neurophysiology, brain function, visual activity

Neuroscience Center
University of Wyoming – P20 RR015640

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Thematic Scientific Focus:
Cellular mechanisms underlying activity dependent changes in central nervous system circuitry and function

Representative Research Projects:
- Activity dependent processing in the fly eye and biologically inspired machine vision
- Daylight regulation of pars tuberalis tachykinin-induced prolactin secretion
- Activity dependent refinement of inhibitory networks in the barrel cortex
- Activity dependent mechanisms of neuropathic pain
-

Research Resources:
- Macromolecular Analysis Facility – real time PCR; nitric oxide analyzer; Versadoc 3000 imaging system with phosphoimager; atrix assisted laser desorption/ionization-time of flight (MALDI-TOF) mass spectrometry; Agilent 8453 UV-Vis spectrophotometer
- Microscopy Imaging Facility – Hatachi TEM with 4K by 4K cooled CCD digital camera (Gatan); Leica and BioRad laser scanning microscopes; epifluorescent microscopes; scanning electron microscope

Index Terms:
neuroscience, neuroplasticity, nociception, somatosensory, neuroendocrine, computational, bioengineering, confocal microscopy, ultrastructure, proteomics

back to top